

AMENDMENTS TO THE SPECIFICATION:

Please replace paragraph [0001] on page 1 after the Title with the following paragraph:

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a divisional of U.S. Serial No. 10/179,373, filed June 26, 2002, now U.S. Patent No. 7,368,285, which is a continuation-in-part of U.S. Serial No. 10/035,045, filed January 3, 2002, now U.S. Patent No. 7,241,880, U.S. Serial No. 09/897,427, filed on July 3, 2001, now U.S. Patent No. 6,955,887, and U.S. Serial No. 09/799,629, filed on March 7, 2001, now U.S. Patent No. 7,244,835; U.S. Serial No. 10/179,373 ~~which application~~ claims priority to U.S. Provisional Application Serial No. 60/300,434, filed on ~~Jun.~~ June 26, 2001, U.S. utility application Ser. No. 09/897,427 filed on Jul. 3, 2001, U.S. Provisional Application Serial No. 60/304,749, filed on Jul. July 13, 2001, U.S. Provisional Application Serial No. 60/310,493, filed Aug. 8, 2001, U.S. Provisional Application Serial No. 60/331,771, filed on Nov. 21, 2001, U.S. Provisional Serial No. 60/339,472, filed Dec. 14, 2001, and U.S. Serial No. 10/035,045 filed Jan. 3, 2002, U.S. Provisional Serial No. 60/372,090, filed Apr. 15, 2002, and U.S. Provisional 60/374,143, filed on Apr. 22, 2002, all of which are incorporated by reference in their entirety.

Please replace paragraph [0038] with the following paragraph:

[0038] Figures 1a-1b contain ~~contains~~ a sequence alignment of human (SEQ ID NOS 5-7) and rat T1Rs (SEQ ID NOS 16-17 & 4), human calcium-sensing receptor (SEQ ID NO: 19) and rat metabotropic glutamate receptor (SEQ ID NO: 18).

Please replace paragraph [0040] with the following paragraph:

[0040] Figures 3a-3c contain data relating to receptor responses to sweet taste stimuli. Figures 3a-3b contain functional data (intracellular calcium responses) elicited by different sweet taste stimuli in HEK cells stably expressing $G_{\alpha 15}$ that are transiently transfected with human T1R2, T1R3 and T1R2/T1R3 at various concentrations of sweet taste stimuli (Figure 3a); human T1R2/T1R3 dose responses for several sweet taste stimuli (Figure 3b); human T1R2/T1R3 responses to sucrose in the presence of gurmarin, and endogenous $\beta 2$ -adrenergic receptor responses to isoproterenol in the presence of gurmarin. Figure 3c contains the normalized response to different sweeteners.

Please replace paragraph [0045] with the following paragraph:

[0045] Figures 8a-8c contains functional data showing HEK cells which stably express $G_{\alpha 15}$ that are transiently transfected with T1R1/T1R3 respond to glutamate in an intracellular calcium-based assay. FIG. 8a shows that intracellular calcium increases in response to increasing glutamate concentration; FIG. 8b shows intracellular calcium responds to IMP (2 mM), glutamate (0.5 mM) and 0.2 mM IMP; and FIG. 8c shows human T1R1/T1R3 responses for glutamate in the presence and absence of 0.2 mM IMP.

Please replace paragraph [0046] with the following paragraph:

[0046] Figures 9a-9b, respectively, contain the results of an immunofluorescence staining assay using Myc-tagged hT1R2 and a FACS experiment showing that the incorporation of the PDZIP peptide (SEQ ID No: 1) enhanced the expression of a T1R (hT1R2) on the plasma membrane.

Please replace paragraph [0047] with the following paragraph:

[0047] Figures ~~10a—10b~~ 10A — 10L contain calcium imaging data demonstrating that hT1R2/hT1R3 respond to different sweet stimuli.

Please amend paragraph [0052] of the specification as follows:

[0052] ~~Figure 16~~ Figures 16A and 16B show that lactisole inhibits the receptor activities of human T1R2/T1R3 and human T1R1/T1R3. Figure 16A shows responses of HEK- $G_{\alpha 15}$ cells transiently transfected with T1R1/T1R3 (circles) to 10mM L-glutamate and HEK- $G_{\alpha 15}$ transiently transfected with T1R2/T1R3 (squares) to 150 mM sucrose in the presence of variable concentrations of lactisole. Figure 16B shows fold increases in taste detection thresholds in the presence of 1 and 2 mM lactisole for the sweet taste stimuli sucrose and D-tryptophan, the umami taste stimuli L-glutamate (MSG) and L-glutamate plus 0.2 mM IMP, and sodium chloride. Detection thresholds were determined following the method of Schiffman et al.

Please amend paragraph [0071] of the specification as follows:

[0071] The invention especially includes biochemical assays conducted using cells, e.g., mammalian, yeast, insect or other heterologous cells that express one or more full length T1R receptors or fragments, preferably N-terminal domains of T1R1, T1R2 and/or T1R3. The effect of a compound in such assays can be determined using competitive binding assays, e.g., using radioactive glutamate

or IMP, fluorescence (e.g., fluorescence polarization, FRET), or GTP γ ³⁵S binding assays. As noted, in a preferred embodiment, such assays will utilize cell lines that stably co-express T1R1/T1R3 or T1R2/T1R3 and a suitable G protein such as G α_{15} . Other appropriate G proteins include the chimeric and variant G proteins disclosed in U.S. Application Serial No. 09/984,292, now U.S. Patent No. 6,818,747, and 60/243,770, incorporated by reference in their entirety herein.

Please replace paragraph [0254] with the following paragraph:

[0254] Additionally, the accession number and reference citations relating to mouse and rat T1Rs and allelic variants thereof in the public domain are set forth below: rT1R1 (Accession # MD18069) (Hoon et al., Cell 96 (4): 541-51 (1999)); rT1R2 (Accession # MD18070) (Hoon et al., Cell 96(4): 541-59 (1999)); mT1R1 (Accession # MK39437); mT1R2 (Accession # AAK 39438); mT1R3 (Accession MK 55537) (Max et al., Nat. Genet. 28(1): 58-63 (2001)); rT1R1 (Accession # AAK07092) (Li et al., Mamm. Genome (12): 13-16 (2001)); mT1R1 (Accession # NP 114073); mT1R1 (Accession # MK07091) (Li et al., Mamm. Genome (12): 13-16 (2001)); rT1R2 (Accession # MD18070) (Hoon et al., Cell 96(4): 541-551 (1999)); mT1R2 (Accession # NP114079); mT1R3 (Accession # AAK39436); mT1R3 (Accession # BAB47181); (Kitagawa et al., Biochem. Biophys. Res. Comm. 283(1):23642 (2001)); mT1R3 (Accession # NP1 14078); mT1R3 (Accession # AAK55536) (Max et al., Nat. Genet. 28(1):58-63 (2001)); and mT1R3 (Accession No. AAK01937).